

WHAT IS CLAIMED IS:

1. A compound to selectively kill a target cell in a patient with reduced systemic toxicity, which comprises a compound of the formula:

W-Z-X

wherein,

X is a therapeutical agent selected from the group consisting of chemotherapeutic agent, antiviral agent, antibacterial agent, antifungal agent and enzyme inhibitor agent;

W is a molecule which is adapted to selectively bind said target cell directly or indirectly; and

Z is a breakable linker which covalently links W and X together, wherein said linked W remains available for binding to said target cell, whereby said breakable linker releases said therapeutical agent into said target cell.

2. The compound of claim 1, wherein said compound when bound to said target cell is internalized into said target cell.

3. The compound of any one of claims 1 and 2, wherein said linker is breakable by pH modification, reduction or enzymatic hydrolysis.

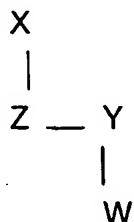
4. The compound of any one of claims 1 to 3, wherein said chemotherapeutic agent is selected from the group of taxanes, taxanes derivatives, anthracyclines, anthracyclines derivatives, doxorubicin, daunomycin, daunorubicin, adriamycin, methotrexate, mitomycin, epirubicin, nucleoside analogs, DNA damaging agents and tyrophostins.

5. The compound of any one of claims 1 to 4, wherein said therapeutical agent is selected from the group of antisense oligonucleotide and cDNA for a gene.

6. The compound of claim 4 wherein said taxane is paclitaxel.

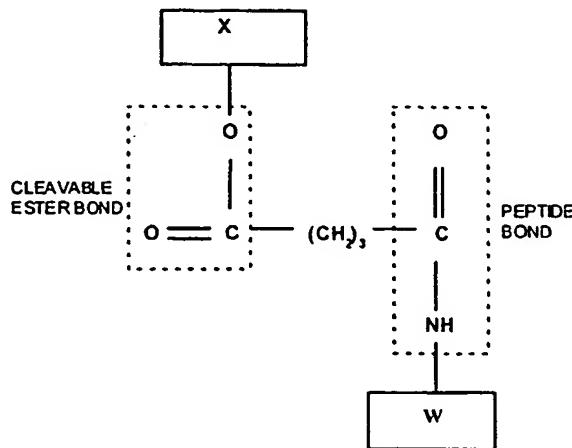
7. The compound of any one of claims 1 to 3, wherein said chemotherapeutic agent is doxorubicin.

8. The compound of claim 1 wherein said molecule is selected from the group of antibody and mimicking molecules thereof, peptides, peptidomimetics, growth factors, hormones, adhesion molecules, viral proteins and functional fragments thereof.
9. The compound of claim 8 wherein said antibody is a monoclonal antibody.
10. The compound of claim 8, wherein said antibody binds to a specific receptor on said target cell.
11. The compound of claim 9 wherein said monoclonal antibody is selected from the group of MC192, 5C3 and a-IR3.
12. The compound of claim 1, wherein said compound further comprises a spacer between W and Z and/or between Z and X.
13. The compound of claim 12, wherein when W is a primary biologically active molecule indirectly binding to said target cell, said compound further comprises W' which is a secondary biologically active molecule selectively bound to W and adapted to selectively bind said target cell.
14. The compound of claim 13 wherein said primary and/or said secondary biologically active molecules is an antibody.
15. The compound of claim 14 wherein a primary antibody is of a species and a secondary antibody is of a different species.
16. The compound of any one of claims 14 or 15, wherein said antibody is a monoclonal antibody.
17. The compound of claim 13 wherein said secondary biologically active molecule is a rabbit-antimouse antibody.
18. The compound of claim 1, wherein said compound is of the formula:

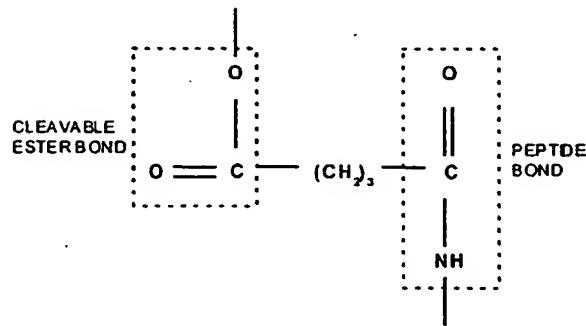


wherein Y is a spacer selected from the group of alkene, alkyl, methyl, ethyl ester, ethyl glycol and $H(CH_2CH_2O)_nOH$, n being between 1 and 90.

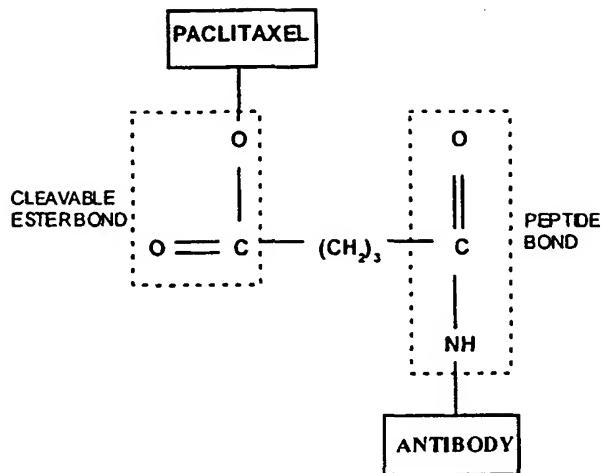
19. The compound of claim 18, wherein said spacer is $(CH_2)_3$.
20. The compound of claim 1, wherein said compound is of the formula I,



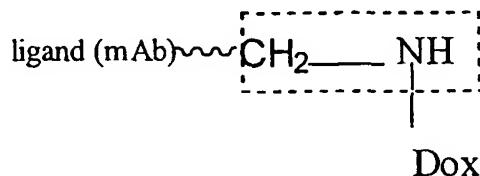
21. The compound of claim 1, wherein Z is



22. The compound of claim 1, wherein said compound is of the formula II,



23. The compound of claim 1, wherein said compound is of the formula III,



24. A therapeutical composition, which comprises a therapeutically effective amount of a compound of any of claims 1 to 23 in association with a pharmaceutically acceptable carrier.

25. An anti-cancer composition, which comprises a therapeutically effective amount of a compound of any of claims 1 to 23 in association with a pharmaceutically acceptable carrier, wherein said therapeutical agent is a chemotherapeutic agent.

26. A method for treating cancer with reduced effects in a patient, said method consisting in administering a therapeutically effective amount of a compound of any of claims 1 to 23 to a patient, wherein said therapeutical agent is a chemotherapeutic agent.

27. Use of the compound of any one of claims 1 to 23 for the manufacture of a medicament for the treatment of cancer with reduced effects in a patient, wherein said therapeutical agent is a chemotherapeutic agent.

28. A method for decreasing toxic side effects and increasing selectivity of a chemotherapeutic agent for tumor cells, said method comprising the step of administering to a patient a conjugate comprising a chemotherapeutic agent conjugated to a molecule which is adapted to selectively bind said target cell directly or indirectly, wherein said compound when bound to said target cell is internalized into said cell and to a breakable linker which covalently links said molecule and said chemotherapeutic agent together, wherein said linked molecule remains available for binding said target cell, whereby said breakable linker releases said chemotherapeutic agent into said target cell.

29. Use of a chemotherapeutic agent conjugated to a molecule for decreasing toxic side effects and increasing selectivity of a chemotherapeutic agent for tumor cells, said molecule being adapted to selectively bind said target cell directly or indirectly, wherein said compound when bound to said target cell is internalized into said cell and to a breakable linker which covalently links said molecule and said chemotherapeutic agent together, wherein said linked molecule remains available for binding said target cell, whereby said breakable linker releases said chemotherapeutic agent into said target cell.

30. A method for by-passing resistance of tumor cells by p-glycoprotein pump (PGP), said method comprising the step of administering the compound of claim 1 to a patient in need of such a treatment whereby said biologically active molecule is a monoclonal antibody and said compound is avoiding membrane diffusion and/or permeability route to enter into said cells.

31. A compound to selectively protect a target cell which comprises a compound of the formula:

W-Z-X

wherein,

X is a protective agent to cells selected from the group consisting of: enzyme inhibitors, ligands of nuclear receptors, vitamin D, vitamin E and analogs thereof, estrogen and analogs thereof and inhibitors of the apoptotic cascade;

W is a biologically active molecule which is adapted to selectively bind said target cell directly or indirectly; and

Z is a linker which covalently links W and X together, wherein said linked W remains available for binding said target cell, whereby said linker releases said therapeutical agent into said cell and whereby said compound is providing a patient with a reduced systemic toxicity.

32. The compound of claim 31, wherein said protective agent is an enzyme inhibitor agent.

33. The compound of claim 32, wherein said enzyme inhibitor agent is a caspase inhibitor agent.

34. A method for decreasing toxic side effects to non-tumor cells, said method comprising the step of administering to a patient a conjugate comprising a protective agent conjugated to a molecule which is adapted to selectively bind said non-tumor target cell directly or indirectly, wherein said compound when bound to said non-tumor target cell and to a breakable linker which covalently links said molecule and said protective agent together, wherein said linked molecule remains available for binding said target cell, whereby said breakable linker releases said protective agent into said cell and whereby said protective agent internalized in said cell is protecting said cell from subsequent toxicity by a chemotherapeutic agent which is therefore decreasing toxic side effects.